Myasthenia Gravis

Problems in Diagnosis

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• **The possibility of myasthenia gravis must be considered in patients persistently complaining of weakness and fatigue. There may be many difficulties and pitfalls in differentiating myasthenia gravis from other disorders in which muscular weakness is a common complaint.**

Observation of a group of 36 patients with myasthenia gravis, and another group of 30 cases involving the differential diagnosis of myasthenia gravis, led to a conclusion that a physician should apply criteria carefully before arriving at a diagnosis of myasthenia gravis and instituting drug therapy, since nonmyasthenics may frequently respond with subjective improvement temporarily following administration of cholinergic drugs.

Myasthenia gravis may be a more common disorder than was suspected in the past.

MYASTHENIA GRAVIS is a disease characterized by muscular weakness. Weakness and the inability to carry out muscular activity is commonly described as fatigue. Fatigue and lassitude are among the most common of human complaints. When they persist and form the basis of the complaint for which a patient seeks medical attention, the diagnosis of myasthenia gravis has to be considered. Because the drugs used in the treatment of myasthenia gravis, in small doses, may give the languid person a "pick up," and because myasthenia gravis may be mild and variable, the differential diagnosis is sometimes difficult; it is always very important.

Myasthenia gravis was first described by Willis in 1672.[16] It has received greater attention since Walker[19] found out in 1934 that the weakness could be reversed by physostigmine. Viets and Schwab[17] in 1935 introduced neostigmine (Prostigmine) in the clinical treatment of this disorder and the neostigmine test as an aid in differential diagnosis.

Diagnosis and treatment have been aided recently by the addition of the edrophonium (Tensilon®) test by Osserman,[10] and by the development of two drugs, pyridostigmine bromide (Mestinon®) and ambenonium chloride[12] (Mytelase®), which are clinically useful in relieving the symptoms.

The exact incidence of myasthenia gravis is unknown but estimates between 50,000 and 100,000 cases in the United States are given by physicians[13] familiar with this disease. In spite of the relative rarity, in the 34-month period between July, 1954, and April, 1957, we had the opportunity of examining 36 patients with the disease at the University of California at Los Angeles medical center. An additional 30 patients were sent to the medical center with the presumptive diagnosis of myasthenia gravis. An analysis of these cases and a brief comparison with the experience and criteria of others form the basis of this report.

The physician must have a constant awareness of the possibility of myasthenia gravis in any patient complaining of muscle weakness and ease of fatigue, despite the recognized nonspecific nature of such symptoms. An accurate history of the patient's symptoms of weakness, including their distribution and variation during the day, as well as response to activity and rest, is essential. A detailed appraisal of the patient's strength and the effect that rapid repetition of effort involving various muscles has with regard to prompt loss of strength is also essential.

Unfortunately, there is no specific test which is consistently reliable for myasthenia gravis. Several may be helpful. Among these are intramuscular injection of neostigmine[18] and intravenous injection of Tensilon.[19] Quinine sulfate[1] may be used at times in doubtful cases in attempt to provoke weakness, but this and curare should probably be used only as a provocative test by physicians fully familiar with the actions of the drugs, and then only with the patient in hospital with facilities available to maintain an open airway and artificial respiration. A myasthenic patient may have pronounced and sudden sensitivity to these drugs, particularly curare.

A placebo control injection is also desirable to evaluate the suggestibility of the patient before giving neostigmine or Mestinon. Atropine, 0.6 mg., is useful for this. It prevents many side effects of cholinergic drugs but has no effect on muscle function at this dosage. Enough time is allowed to elapse following the administration of the atropine or other placebo to redetermine the patient's complaints and muscle strength. The neostigmine test is done by giv-

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ing 1.5 mg. of the drug intramuscularly and then reappraising the patient's complaints and strength at intervals of 10 minutes for the next one to two hours. Improvement is usually seen within 20 to 40 minutes and may last several hours.

For the Tensilon test the drug is administered cautiously intravenously in amounts of from 2 to 10 mg. Complaints and muscle strength are observed at one or two minute intervals for the next 10 minutes. This drug acts rapidly—within one to five minutes. Toxic effects of neostigmine and Tensilon include increased salivation, abdominal cramps, urinary frequency, diarrhea, muscle twitching and muscle cramps, choking sensations, miosis and muscle weakness.

Barium swallow during fluoroscopic examination, electromyographic[3] studies, attempts to evoke the Jolly reaction by faradic stimulation, and ergographic tracings are helpful adjuncts. These may also be combined with the neostigmine or Tensilon tests. Each requires special equipment and experience. None is entirely conclusive.

It is essential that patients have demonstrable muscle weakness before the neostigmine or the Tensilon test is carried out. These tests generally are not applicable when the patient is in a remission or has recently received extensive amounts of cholinergic drugs. The use of a hand dynamometer may be helpful in assessing improvement in the patient's strength.

Frequently patients with asthenia on an emotional or psychic basis will for a time have subjective improvement and feeling of well-being in response to cholinergic drugs. This may also occur in patients who have muscular or neurological disorders of other sorts, but the effect is not consistently sustained and does not have accompanying objective evidence of improvement. This "boost," "pick-up" or nonspecific response may often be confusing to physicians unfamiliar with these test procedures and may lead to erroneous diagnosis of myasthenia gravis.

MATERIAL OF STUDY

We reviewed the records of the patients with problems of weakness who were observed by us in the division of neurology at a new University Medical Center between July, 1954, and April, 1957. There were 66 patients with these complaints in whom the possibility of myasthenia gravis was raised. Fifty-seven had had a diagnosis of myasthenia gravis made on the outside. In 34 cases this was confirmed. Two patients with other diagnoses were later found to have myasthenia. Twenty-five patients had weakness from some other cause. In five cases the diagnosis was considered doubtful.

Of the 66 patients, 54 previously had received neostigmine or other anticholinesterase drugs for a week or longer. Although the diagnosis of myasthenia was made in more cases than it actually could be confirmed, among the patients who did have the disorder, in only three cases was the diagnosis made within one month of onset of the first symptom. The delay between onset of first symptoms and diagnosis of myasthenia gravis in persons with confirmed diagnosis varied from less than one month to 23 years (Table 1). There were 21 females and 15 males in the myasthenic group. The age at onset of first symptom ranged from 15 to 69 years. Relatively early onset in females and later onset in males observed in this series (Table 2) is in agreement with data gathered by other observers.

Fourteen patients had a single initial symptom. More frequently they complained of weakness in two or more muscles simultaneously or in prompt succession. The most common symptoms were drooping of the eyelids and double vision (Table 3).

Drooping of the eyelids and double vision predominated, in both females and males, over all other

TABLE 1.—*Lapse of Time Between Onset of First Symptoms and Diagnosis of Myasthenia Gravis, in Confirmed Cases*

	Females	Males
Less than 1 month	1	2
1 month	2	2
2 to 3 months	2	3
4 to 6 months	4	1
7 to 12 months	5	4
2 years	2	1
3 years	3	—
4 years	1	—
20 years	—	1
23 years	—	1

TABLE 2.—*Age of Patients at Onset of Myasthenia Gravis*

	Females	Males
11 to 20 years	5	1
21 to 30 years	9	2
31 to 40 years	3	4
41 to 50 years	2	1
51 to 60 years	1	3
61 to 70 years	1	4

TABLE 3.—*Various Conditions Appearing as Presenting Symptoms in 36 Patients with Myasthenia Gravis. (More than a single symptom in some cases.)*

	Females	Males
Ocular ptosis	8	6
Diplopia	9	6
Jaw weak	1	3
Face weak	2	1
Voice weak	5	2
Dysphagia	2	—
Arms weak	3	1
Hands weak	3	—
General weakness	3	3

symptoms that appeared at any time in the 36 cases (Table 4).

As to the site of muscle weakness at the time of examination, ptosis and diplopia or limitation of one or more of the extraocular muscles predominated (Table 5). Of particular interest was the observation of hypoactive reflexes in seven cases, and moderate to pronounced muscle wasting or atrophy in four females.

In retrospect, the diagnosis of myasthenia gravis seems simple from the history of fluctuating muscle weakness, particularly involving the cranial nerve musculature. This weakness increases with activity and incompletely improves with rest. The weakness also is lessened by giving anticholinesterase drugs. The following two cases illustrate delay and confusion regarding the diagnosis.

CASE 1. A 47-year-old man had had weakness of muscles for 23 years, beginning with transient double vision and facial weakness after a minor cranial injury, without loss of consciousness, while in military service. The patient also noted general weakness, drooping of the eyelids, sore, aching neck, difficulty in swallowing, difficulty in talking and sometimes weakness of the upper right extremity. On at least five occasions he had had remission of all symptoms for periods of a few weeks to several years. There was a history of perforated duodenal ulcer. The patient continued to work regularly despite the symptoms, which were never severe.

Upon examination, a fluctuating ptosis was noted, at times greater in the left than the right eye. There was bilateral variable limitation of extraocular movements. Mild to moderate muscle weakness in the left shoulder girdle and triceps was noted. A neostigmine test done elsewhere (the first in 23 years since the onset of symptoms) gave prompt relief of muscular weakness. The patient had good response to continued therapy with neostigmine and Mestinon by mouth.

CASE 2. A 65-year-old surveyor was unable to bite through his usual noon-day salami sandwich. Each succeeding bite was weaker and he had to close his mouth with his hand. He could not hold his pipe between his teeth. Soon he had difficulty in holding his head erect, along with transient double vision, weakness of voice, inability to extend the fingers and weakness in the legs on climbing about the hills while surveying. All symptoms fluctuated and were worse after exertion.

An intramuscular Tensilon test was done elsewhere and the result was interpreted as negative. The following day the symptoms were worse and the patient attributed the deterioration to the test. He was considered to have hysteria. He sought additional opinion. The patient had had a toxic goiter removed six years previously.

Upon examination by us, ptosis and weakness of the jaw, face and neck musculature were noted. The deltoid muscles were also weak. Repeated tests elicited increasing weakness of the thigh flexors. There was no evidence of hyperthyroidism. An intravenous Tensilon test gave prompt relief of the symptoms and signs. The relief lasted about 25 minutes and was followed by increased symptoms. Later Mestinon was given by mouth and the therapeutic response was good.

It is to be noted that the first Tensilon test in this case was done by giving the drug intramuscularly, an unsatisfactory method and probably the reason for the "negative result."

TABLE 4.—*Incidence of All Symptoms Noted at Any Time in 36 Cases of Myasthenia Gravis*

	Females	Males
Ocular ptosis	14	12
Diplopia	19	13
Jaw weak	10	10
Face weak	2	5
Voice weak	14	11
Dysphagia	15	10
Neck weak	1	2
Arms weak	12	6
Hands weak	9	4
Respiratory difficulty	6	4
Legs weak	9	6
General weakness	12	7

TABLE 5.—*Incidence of Muscle Weakness at Various Sites Noted at First Examination of 36 Patients with Myasthenia Gravis*

	Females	Males
Ocular ptosis	15	12
Diplopia	13	12
Jaw weak	8	6
Face weak	14	8
Voice weak	10	4
Dysphagia	2	2
Neck weak	5	5
Arms weak	13	11
Hands weak	9	7
Respiratory difficulty	1	—
Legs weak	13	6
General weakness	5	3
Atrophy	4	—
Hyporeflexia	4	4
Ocular proptosis	1	1

In a second group of five cases it was doubtful whether the patient had myasthenia gravis currently, had had the disorder in the past (being presently in a state of remission) or had some other disorder. There were three females and two males in this group. The age range was 24 to 60 years. Duration of symptoms ranged from two to eleven years. All had received neostigmine or other similar drugs. Two complained of double vision, one of feeling tired, one of weakness in the hand and difficulty in writing, and one of arm weakness and buckling of the knees. Two cases illustrate the difficulties of diagnosis in such instances.

CASE 3. A 49-year-old housewife and former telephone operator had a history of easy fatigue and tiredness for 12 years. On several occasions she had collapsed suddenly and had been unable to talk. She

said that sometimes her muscles "would not obey." At times she had a feeling of heaviness in the stomach and chest and she had difficulty breathing. Climbing stairs was also difficult. Her vision was intermittently blurred and she had pins-and-needles sensation on her neck. She had worried about her heart in the past. A diagnosis of myasthenia gravis had been made four years previously, and she then had begun taking neostigmine, up to 22 tablets (15 mg. each) daily. Later she combined this amount of neostigmine with four Mestinon tablets (60 mg. each) daily. She did not have clear-cut relief. Occasionally she felt nauseated and dizzy.

On examination she was observed to be obese. She sighed frequently. There were occasional twitchings of the eyelids and the grip of the hands felt slightly weak, but there was no other clear weakness on repeated effort or other neurological abnormality.

It was believed that she had mild cholinergic intoxication. We recommended she gradually discontinue use of neostigmine and Mestinon. She was observed for a two-month period, but she did not reduce the dosage of neostigmine below 15 tablets daily since it seemed to relieve her subjective feelings of exhaustion. There was no evidence of increased weakness at the lower dose. No changes in condition were noted over the period of observation and she continued to complain of blurred vision and nausea.

A definite diagnosis in this patient could not be made. It was not possible to differentiate cholinergic intoxication, myasthenia gravis, myasthenia gravis in remission or asthenia of undetermined cause associated with emotional problems. She refused to give up neostigmine and continued to take sizable doses. Asthenia of undetermined cause seemed a likely possibility.

CASE 4. A 39-year-old unemployed, married salesman noted intermittent double vision 11 years earlier. At 17 and 22 years of age he had had head injuries, with unconsciousness both times, but without immediate sequelae. Six years earlier he had a series of three operations on the extraocular muscles in an attempt to correct intermittent, convergent squint. These were only briefly successful in relieving double vision. Five years earlier the diagnosis of myasthenia gravis was made elsewhere and neostigmine was prescribed. At first the patient noted improvement. He increased the dosage gradually up to 80 tablets (15 mg. each) a day. Then he began to have episodes of muscle soreness, twitching, breathlessness, cramping, weakness, tightness in the throat, failing voice, difficulty in breathing and occasional abdominal cramps and sweating. He also took ephedrine, racemic amphetamine (Benzedrine), dextroamphetamine (Dexedrine) and betaine glycocyamine (Betasyamine) in varying amounts. He was given corticotropin (ACTH) and acetazoleamide (Diamox), following which he had transient, sudden "remission" of all symptoms for three and a half weeks. He had not worked for over a year.

On examination he was observed to be muscular. He was very talkative and he sighed frequently. He had variable exotropia and horizontal nystagmus on lateral gaze to either side. Convergence was impaired. The right palpebral fissure was slightly wider than the left There was no ptosis. Frequent twitches of the eyelids and masseters were present. There was no evidence of muscle weakness.

The gait was bizarre, with deep bending of the knees and reeling and staggering from wall to furniture. When walking the patient sighed deeply, breathed laboriously and complained of exhaustion. Results of nonequilibratory coordination tests were normal.

When it was suggested that he might not have myasthenia gravis and should reduce the amounts of drugs he was taking, he became quite agitated, critical and difficult. He had several interviews in the psychiatric clinic. Gradually and with protest, he reduced the use of drugs and finally stopped taking them. He telephoned at odd hours, relating that he was in a state of collapse and couldn't get his breath, even as he continued to talk in a loud, clear voice for periods up to 45 minutes. When use of the drugs he had been taking finally was stopped, muscle twitches ceased. The disturbance in extraocular movements was unchanged. He showed no other muscle weakness. After a few weeks had elapsed he attempted to resume use of neostigmine when he felt weak. Cramps, sweating and diarrhea promptly ensued. He made no subsequent attempts.

In this patient it was impossible to clearly differentiate among myasthenia gravis relatively localized to the extraocular muscles, myasthenia gravis in remission, hysterical convergence spasm, intermittent diplopia from some other cause, cholinergic crisis, other manifestations of hysteria and conversion, the effects of previous operation on eye muscles and asthenia of undetermined cause. It was obvious that emotional or psychological factors were prominent, although not exclusive.

A third group of 25 patients did not have myasthenia gravis. In this group there were 23 females and two males. Nineteen had had diagnosis of myasthenia gravis elsewhere. Seventeen had received anticholinesterase drugs for a significant time. The initial symptoms or complaints were similar to those noted in the patients who had myasthenia gravis, but were more diversified. Eleven patients complained of fatigue, tiredness, lack of energy; three of general weakness; two each of transient double vision, drooping eyelids, voice disturbance, weak arms, weak legs and "myasthenia gravis"; and one each of inability to use extremities after sleep, frequent blinking, muscle tightness in thighs and legs, difficulty in walking since childhood, sudden shakes, shakiness of legs, alterations of consciousness, itching and peeling of lips, and nervousness. Details of all of the complaints and findings were so diverse and extensive as to be of no value; they constituted a heterogeneous group of disorders

(Table 6). Eleven of this group, all of them females, had asthenia of undetermined cause. In two cases these complaints had existed for more than six and less than twelve months. In nine cases they had existed for longer periods—from four to forty years. In none was there clear-cut evidence of objective neurological, muscular or metabolic defect to account for the subjective complaints of weakness. Nine of the eleven patients had received neostigmine therapy.

Difficulties in differentiating the myasthenic from other disorders is illustrated by the following cases:

CASE 5. A 47-year-old housewife from a distant town was transferred to the hospital at the University of California at Los Angeles medical center by ambulance with a chief complaint of "myasthenia gravis." She had a history of easy fatigability and intermittent difficulty in walking since childhood. As a child she wore braces on her legs. She fell frequently in her teens. On direct questioning she admitted occasional double vision. Five years earlier she was considered to have myasthenia gravis. She began taking neostigmine by mouth and noted transient improvement in symptoms. She continued to have feelings of general weakness, for which she took additional neostigmine. This was frequently followed by tight feelings in the muscles of the throat, choking sensation and difficulty breathing for which she received oxygen inhalation therapy. Before admittance to hospital, she had remained in bed for six months following collapse at the time of extraction of a tooth. During the three months immediately preceding admittance she had a chronic cough and more frequent choking spells. She was taking 12 tablets of neostigmine (15 mg. each) and 12 tablets of Mestinon (60 mg. each) daily when admitted.

Upon examination the patient was observed to be tense, anxious and tremulous. The pupils were miotic. Early clubbing of the fingers and toes was noted. Strength was poorly sustained but improved with repeated testing and encouragement. X-ray films of the chest showed a sharply delineated mass in the anterior aspect of the right mid-lung field.

Use of neostigmine and Mestinon was discontinued within two days. The patient had no loss of strength and became ambulatory for the first time in six months. The pupils became larger.

Right upper lobectomy was done at another hospital and adenocarcinoma with spread to the hilar nodes was diagnosed. The patient died three months later of metastasis.

CASE 6. A 51-year-old woman, a professor of art, some three months before admittance to hospital, noted tightness in the legs and thighs, followed by weakness making it difficult for her to operate her car. Her back, trunk and upper extremities became weak within the next two weeks. She was admitted first to another hospital and there had difficulty in chewing, swallowing and talking. She was considered to have myasthenia gravis and administration of neostigmine and Mestinon was begun. Nausea, vomiting, diarrhea, muscle twitching and cramps developed, without improvement in strength. X-ray, 500 r, was given over the thymus, then corticotropin (ACTH) and cortisone. Slight improvement followed. In the course of further examination a mass in the left breast was noted. She said the lump had been present for four years. Biopsy revealed carcinoma. Intensive x-ray therapy to the breast and axilla was given. Then testosterone was administered. Strength slowly improved and the patient was referred to us for confirmation of myasthenia gravis three months later. She had spent considerable time lying in the sun.

Questioning elicited an episode of "nonparalytic polio" four years earlier, during which there were no abnormalities in the spinal fluid. Thereafter the patient had soreness, stiffness, tightness and slight weakness in the thighs, which responded to hot packs and physiotherapy over a period of four months.

Upon examination the patient was noted to be well "tanned." Also noted were general moderate muscle atrophy and constant weakness involving the face, neck, shoulder girdle, forearms, pelvic girdle and legs. Bilateral foot drop was observed. The deep tendon reflexes were absent in the upper extremities. The ankle jerks were 2 plus. There was no sensory defect. No satisfactory diagnosis was immediately reached. The patient continued to gain strength in the legs and resumed teaching, but six months later she returned with pain in the shoulders, worse on the left, and difficulty in holding her head erect. An electromyogram elsewhere was considered consistent with muscular dystrophy with a myotonic component. At that time there were contractures limiting abduction of the arms, and the shoulder girdle weakness was greater than before, especially on the left. There were no abnormal masses felt in the axilla. Sensation was intact. The left subacromial region was tender. The patient's head hung forward. The skin remained deeply "tanned" although she had not been in the sun for several months. The

TABLE 6.—*Diagnoses in 25 Nonmyasthenic Cases*

Myotonia atrophica with hyperthyroidism and thyrotoxic myopathy.
Bulbar amyotrophic lateral sclerosis.
Bulbar and cervical amyotrophic lateral sclerosis.
Familial external ophthalmoplegia.
Nonfamilial external ophthalmoplegia with atypical muscular dystrophy.
Dermatomyositis and carcinoma of breast.
Probable brain stem infarction and known coronary occlusion.
Old pulmonary (Tbc.), hypertensive cardiovascular disease, diabetes mellitus, and arteriosclerosis.
Habit spasm of blinking and old herpes zoster of face.
Narcolepsy with sleep paralysis and possible cataplexy.
Probable temporal lobe seizure with old head injury and superimposed hysterical weakness.
Probable sleep paralysis, chronic cough and breathlessness on neurotic basis.
Simple senile mental deterioration and atrophic dermatitis.
Postinfectious asthenia.
Asthenia of undetermined cause (11 cases).

dorsum of the hands, fingers and knees were erythematous and rough. The possibility of dermatomyositis was considered and later was proved by muscle and skin biopsy in the hospital. Meticorten was given to her as an outpatient and reduction in pain and improvement in strength ensued.

Ten months later the patient slipped and fell at school, receiving an intertrochanteric fracture of the right hip. She was admitted to the hospital again. Nailing was done at the site of fracture. A skeletal x-ray survey showed no metastatic neoplastic lesions. The patient resumed walking unaided two months later and returned to her teaching duties.

This case illustrates the association of dermatomyositis and malignant disease. In this the neoplasm was carcinoma of the breast. The weakness was initially confused with that of myasthenia gravis. It is quite possible that the episode of "nonparalytic polio" four years earlier was the onset of the polymyositis and that there was then spontaneous remission. When the next episode occurred, her condition improved with the administration of corticotropin, cortisone and, later, meticorten. However, she had also received intensive x-ray therapy, as well as testosterone, which may have had some influence. Spontaneous remission cannot be excluded.

DISCUSSION

These cases illustrate only a few of the problems facing a physician attempting to unscramble and relieve the patient's complaint of muscle weakness and fatigue of various sorts with particular relation to myasthenia gravis. Among other disorders which may be considered in differential diagnosis, to make a partial list, would be: Amyotrophic lateral sclerosis, adynamia episodica hereditaria, botulism, cholinergic crisis, catalepsy, dermatomyositis, familial periodic paralysis, hyperparathyroidism, hyperthyroidism, multiple sclerosis, myotonia atrophica, narcolepsy, polymyositis, polyneuropathy, primary aldosteronism, progressive external ophthalmoplegia, progressive muscular dystrophy and psychoneurosis with asthenic reaction. At times more than one disorder may be present. Our findings and criteria, although in a relatively small series, are in general agreement with those of larger series reported by Schwab and Leland,[14] Hoefer and co-workers,[6,11] Eaton and co-workers,[2] Grob and Harvey[5] and Turner.[15]

The initial complaints in myasthenic persons are often attributed to emotional stress and exhaustion because of their fluctuating evanescent nature. At first the patient may feel tired or more easily fatigued than usual. He may have sudden drooping of one or both eyelids. Transient double vision is another early complaint. Facial weakness with inability to smile or whistle, and lack of facial expression are common. Women find it hard to raise their hands and arms over their heads to put up their hair or remove and replace housewares on high kitchen and closet shelves. Walking and climbing stairs may be increasingly difficult as the task is continued, only to become somewhat easier after a short rest. Trouble in chewing, swallowing, talking and keeping the mouth closed are other frequent symptoms which increase with continued effort. The voice gradually fades with continued talking. The patient may have difficulty keeping the head erect and find that he can flex but not extend the fingers. More severely affected patients may be unable to swallow oral secretions, or cough or breathe adequately. No muscle group is immune.

The weakness is increased with activity and improves incompletely with rest, only to recur with further activity. In women, weakness usually is greater just before or at the time of the menses. Infections, fevers and emotional stress are often accompanied by increased weakness. At first weakness of only one eye muscle or other muscles served by cranial nerves is present for a few days or weeks. Then this weakness may disappear entirely for several months or years, only to recur in more pronounced form with additional weakness elsewhere.

Although the patients may be severely weak and apprehensive, they often appear deceptively passive and calm. This is attributable to the weakness of the muscles controlling facial expression, the voice and extremities through which overt evidence of anxiety and acute difficulty are commonly manifested. The tendon reflexes are normal or somewhat reduced in severely involved muscles.

The exact cause of myasthenia gravis is unknown. The current theory[8] and studies indicate it is due to a variable defect in the electrochemical mechanism by which the nerve impulse is transmitted to the muscle at the neuromuscular junction. This is often likened to the neuromuscular block produced by curare, but differs from it in several respects.

There are no specific pathological changes in the nervous system or muscle as determined by usual laboratory techniques. Collections of lymphocytes, called lymphorrhages, are occasionally seen in the muscles. Thymic enlargement or thymoma is seen in about half of the patients.[2,4,9]

It is a disorder mainly of young women and older men, but may occur at any age. Sixty-four per cent of the women have the first symptoms before 30 years of age, and 74 per cent of men after that age.[14]

Neonatal myasthenia may occur in infants of myasthenic mothers. It is transient and responds favorably to therapy, which may be life saving.

Since failure to recognize and treat myasthenia gravis or treating another disorder as myasthenia gravis with antimyasthenic drugs may involve serious risks to the patient and confuse the physician with additional symptoms, it seems worthwhile to

reconsider means for improving diagnostic accuracy.

The concept that nonmyasthenic persons are unable to tolerate large doses of neostigmine or other similar drugs is not substantiated in our experience. Many of the patients we observed with complaints of weakness in association with psychoneurosis built up to large doses in attempting to overcome their subjective symptoms. Some had moderate to severe side effects at intervals. None showed any frank evidence of increased weakness on rapid withdrawal of the drugs. Some insisted on continuing use of the drugs as a psychological crutch.

On the other hand, it is well known that the course of myasthenia gravis may fluctuate widely, as well as the need for antimyasthenic drugs. Not uncommonly a patient with myasthenia gravis who once required large doses is still taking them even though when examined they have good strength or even signs of mild cholinergic intoxication.

Reliable diagnosis of myasthenia gravis may be made only after the physician obtains an accurate history of the patient's complaints and problems, along with a careful physical and neurological examination, supplemented by appropriate laboratory examination and tests. It is always desirable to reach a prompt diagnosis, but the decision that the patient has myasthenia gravis should not be made until after all evidence has been weighed and carefully appraised. Cholinergic or anticholinesterase therapy should be given on the basis of positive, objective findings rather than subjective findings. The use of such medication for supportive therapy in patients with other disorders is hazardous and should be discouraged.

The advent of previously mentioned new drugs for the diagnosis and relief of symptoms in myasthenia gravis, the increased interest in neurochemistry and in neuromuscular transmission, along with the general absence of degenerative changes in myasthenic persons, make the future seem bright for patients with this disorder.

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